MAJOR ARTICLE

Use of Stool Collection Kits Delivered to Patients Can Improve Confirmation of Etiology in Foodborne Disease Outbreaks

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Background. In 68% of foodborne disease outbreaks, no etiologic pathogen is identified. In two-thirds of outbreaks with no identified etiology, no stool specimens are submitted for testing.

Methods. From April 2001 to March 2003, we pilot-tested use of prepackaged, self-contained stool specimen collection kits in 3 states, delivered to and from patients by courier or mail, to improve rates of specimen collection in the outbreak setting. Specimens were tested for bacterial and viral pathogens at health department laboratories, and results were correlated with epidemiological investigation data.

Results. Specimens were returned by ⩾1 person in 52 (96%) of 54 outbreaks in which kits were deployed; in total, 263 (76%) of 347 persons who received kits returned specimens. Resolution of symptoms was the most commonly cited reason for nonsubmission of kits. An etiology was confirmed in 37 (71%) of 52 outbreaks with specimens returned; 28 (76%) were attributable to norovirus, and 9 (24%) were attributed to bacterial pathogens. Stool kits were well received and cost an average of ~$43 per specimen returned.

Conclusions. In two-thirds of foodborne disease outbreaks in which delivered stool collection kits were successfully deployed, an etiologic organism was identified. Delivery of kits to and from patients to improve rates of stool collection in outbreaks in which specimens might otherwise not be submitted could substantially reduce the number of outbreaks with an unknown etiology.

Foodborne diseases cause an estimated 76 million illnesses and 5000 deaths in the United States each year [1]. In 2001, 1238 outbreaks of foodborne disease were reported to the US Centers for Disease Control and Prevention (CDC; Atlanta, GA), of which 63% did not have a confirmed etiology. The proportion of foodborne disease outbreaks reported to the CDC without a confirmed etiology has not changed substantially during 1990–2001, averaging ~65% (range, 55%–73%) each year [2]. During this period, bacterial pathogens caused most outbreaks with a confirmed etiology, accounting for an average of 72% of such outbreaks.

Norovirus (previously referred to as "Norwalk-like virus" or "small round-structured virus"), a calicivirus, is thought to account for two-thirds of foodborne gastroenteritis in the United States [1]. As molecular diagnostics for noroviruses are becoming more widely available in state public health laboratories, these agents are accounting for an increasing proportion of reported foodborne outbreaks with a confirmed etiology. For example, noroviruses accounted for 8% of outbreaks of foodborne infection reported to the CDC during 1997–2001, compared with 1% of outbreaks reported during 1992–1996. However, even with increased diagnostic capacity at state public health laboratories, the proportion of outbreaks of foodborne infection attributable to noroviruses in the United States remains lower than in many other countries, suggesting continued underreporting of outbreaks of norovirus infection, compared with reporting of outbreaks of infections with bacterial etiologies [3, 4]. A greater underreporting of outbreaks of norovirus infection in the United States

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is supported by data indicating that the incubation period and the duration of illness of a high proportion of foodborne outbreaks reported to the CDC without a confirmed etiology are consistent with the incubation period and duration of illness for noroviruses. Furthermore, a recent review of outbreaks reported in Minnesota indicated that noroviruses accounted for 41% of outbreaks of foodborne infection during 1981–1998 [5, 6].

Increasing the proportion of outbreaks of foodborne infection with a confirmed etiology will help refine strategies for the prevention and control of foodborne disease outbreaks and allow targeting of interventions against the most common etiologies. An etiologic agent may not be confirmed in a outbreak of foodborne infection for several reasons, including limited health care–seeking behavior of ill persons, limited collection or testing of specimens, lack of access to appropriate diagnostic tests, delayed reporting, and limited resources and competing priorities in health departments. An analysis of foodborne disease outbreaks reported to the Foodborne Diseases Active Surveillance Network (FoodNet) in 1998 and 1999 showed that no stool specimens were collected for laboratory testing in two-thirds of outbreaks of infection for which there was not a confirmed etiology [7]. In the absence of adequate stool specimens, improved laboratory testing techniques and enhanced surveillance activities cannot increase the proportion of outbreaks of infection with a confirmed etiology. Potential barriers to successful collection of stool specimens include delays in requesting specimen collection from ill persons, lack of easy-to-use collection materials and instructions, and inconvenience associated with storing and transporting specimens to the laboratory.

Although investigating outbreaks is a fundamental health department function, we are unaware of published studies that address specific methods of overcoming the barriers to successful specimen collection. We conducted a 2-year pilot study at 3 FoodNet sites to test the hypothesis that use of self-contained stool collection kits delivered to and from the homes of patients associated with foodborne disease outbreaks would improve outbreak investigations by facilitating recovery of stool specimens from patients. Our study also allowed an assessment of the etiologic role of noroviruses in outbreaks of foodborne infection by ensuring that all specimens were tested for this agent by means of sensitive molecular diagnostics.

METHODS

The study was performed from April 2001 through March 2003 in Tennessee and selected counties in California (Alameda, Contra Costa, and San Francisco counties) and Maryland (Anne Arundel, Baltimore, Harford, Howard, Montgomery, and Prince George's counties). Stool collection kits were packaged and distributed by state health department staff to regional and county epidemiologists for use during investigations of suspected foodborne disease outbreaks within their jurisdictions. Any outbreak in the study area meeting the CDC case definition of a foodborne disease outbreak was eligible for inclusion in the study [8]. Delivery of the stool collection kits directly to patients was intended to supplement existing local, regional, and state health department investigation protocols. Health department staff were encouraged to use the kits to obtain stool specimens from persons associated with foodborne disease outbreaks who likely would not have submitted stool specimens without the kits (for example, persons who did not seek medical care or would not travel to and from the health department). A maximum of 1 kit was dispensed to each case patient.

Stool collection kits included transport media, instructions, and necessary supplies for specimen collection and transport. Kit composition varied slightly in each state. In Tennessee, the kits included latex gloves, a plastic trash bag, a paper stool collection "hat" for use on a toilet seat (Protocult; ABC Enterprises), a plastic transport container with attached prepaid mailing label, a sealable plastic bag, cotton padding, a ParaPak liquid medium specimen collection tube with self-contained specimen spoon (Meridian Diagnostics), specimen labels, and illustrated instructions (figure 1). In Maryland, the stool collection kit included a plastic hat and a specimen container with a scoop but no transport media. In California, an additional specimen collection container was included for testing for viruses (Kendall Precision; Forrest Biomedical and Environmental Laboratories).

The methods of delivery and receipt of kits to and from patients also differed between the sites. In Tennessee, kits were delivered to participants by health department personnel, commercial courier (in metropolitan areas), or US mail (in rural areas). Specimens were returned by the participant to the state public health laboratory by commercial courier or US mail. In California, kits were delivered to and picked up from participants by commercial or health department couriers. In Maryland, a courier was paged by the local health department to deliver kits to the participants or laboratory. In each state, a health department staff person was assigned to be the primary contact person to coordinate delivery of the stool collection kits to patients and laboratories. This person contacted the patients and notified the commercial or public health department courier to arrange for transport and handling of kits. Efforts were made to deliver and collect kits at locations (such as home or workplace) and times (including evenings and weekends) convenient for each patient. Patients were given the option to deliver the kits in person at their discretion.

Stool specimens received at county or state public health laboratories were tested for bacterial pathogens by use of standard local protocols and for noroviruses by RT-PCR testing.

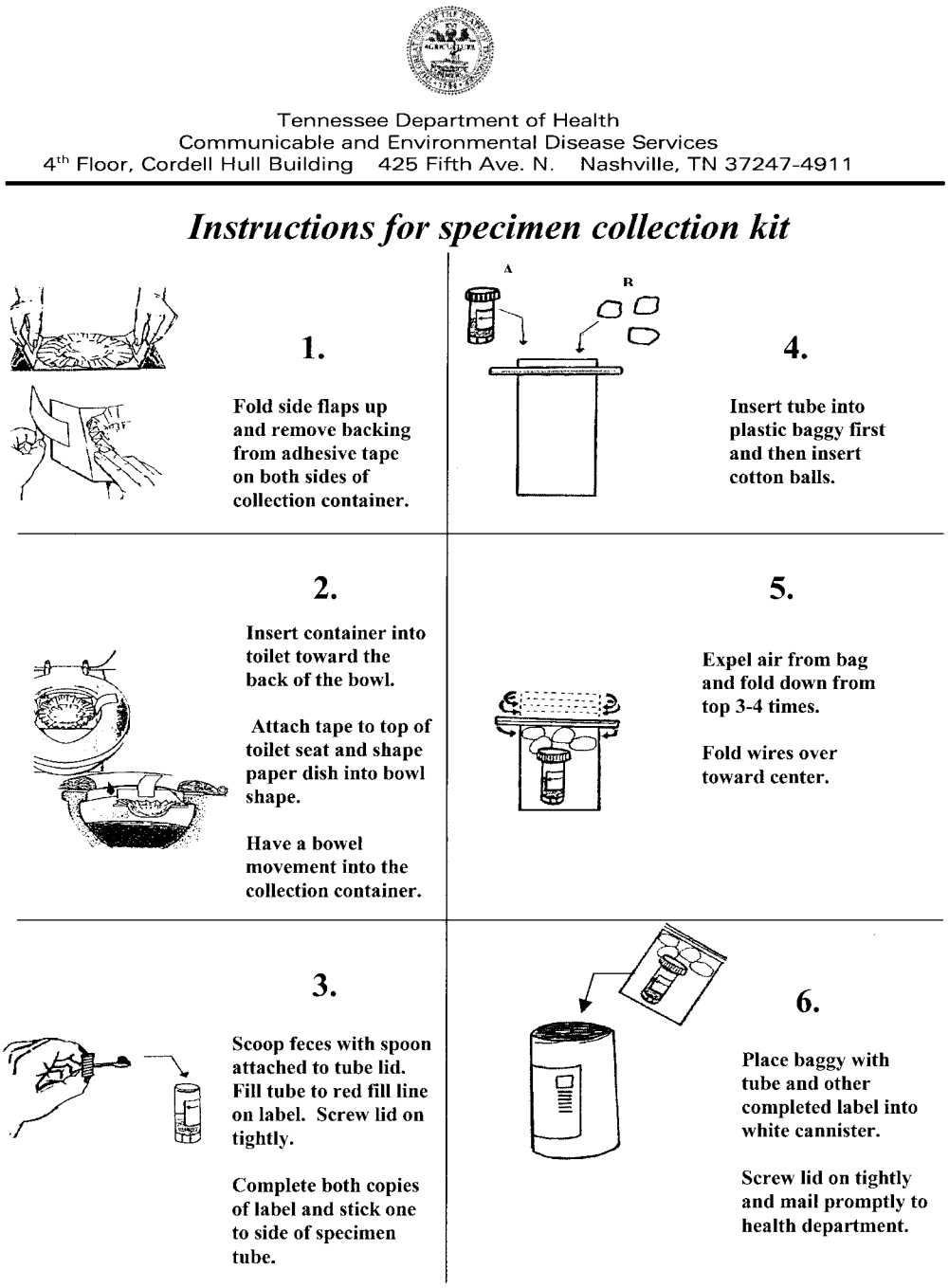

Figure 1. An example of the illustrated instruction sheets included with specimen collection kits sent to persons involved in foodborne disease outbreaks. Spanish-language instructions were also available.

Laboratory testing protocols were not changed during this study. Laboratories in all 3 states tested for noroviruses.

Costs of using stool collection kits were estimated at each site. Costs included materials and staff time for assembly of kits, costs of mailing or courier delivery, and health department staff time devoted to transporting or handling kits.

After each outbreak investigation, health department staff attempted to contact all persons to whom kits were sent to

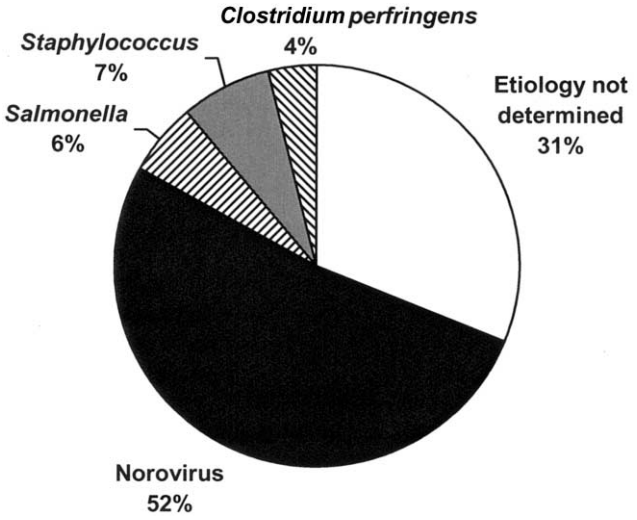

Figure 2. Laboratory-confirmed etiologies of infections in 54 outbreaks in which stool collection kits were deployed.

administer a structured telephone survey asking for their opinions on the kits and their components, ease of use, barriers to use, and reasons why kits were not returned.

RESULTS

During the 24-month study period, stool collection kits were deployed in 54 outbreak investigations at the 3 sites (28 outbreaks in Tennessee, 14 in Maryland, and 12 in California), and specimens were returned from ⩾1 affected person in 52 outbreaks (96%). Overall, stool collection kits were delivered to 347 persons associated with the outbreaks, of whom 263 (76%) returned kits with a stool specimen. The median number of kits distributed per outbreak was 5 (range, 1–42). The median number of kits returned with stool specimens per outbreak was 4 (range, 0–33). Of kits returned to the laboratory, 48% were delivered by commercial courier, 24% by US mail, 23% by health department or laboratory courier, and 5% by the patient themselves.

An etiologic agent was confirmed in 37 (71%) of the 52 cases in the outbreaks in which ⩾1 kit was received at the laboratory. A single pathogen was identified in specimens with positive test results from each outbreak except 1, in which norovirus and *Clostridium difficile* were identified in samples from different patients. Therefore, an etiology was confirmed in 69% of outbreaks of infection in which the stool collection kits were deployed. Of these, 28 (76%) were attributable to norovirus, and 9 (24%) were attributed to bacterial pathogens (figure 2). In the 2 years before this study, only 50% of infections in outbreaks reported in these sites had a confirmed etiology. Characteristics of outbreaks of infection with a confirmed etiology and of those without a confirmed etiology were compared (table 1). Although stool collection kits tended to be returned more frequently and more promptly in outbreaks of infection with a confirmed etiology than in those without a confirmed etiology, the differences were not statistically significant. Stool kits returned by courier were more likely to be associated with outbreaks of infection with a confirmed etiology than were kits returned by other methods of transport. An etiology was not confirmed in 17 outbreaks of infection in which stool kits were deployed; 10 (59%) of these had ⩽3 kits submitted, compared with 16 (43%) of 37 outbreaks of infection with a confirmed etiology ($P = .29$). Other possible reasons for failing to confirm the etiology of infection in outbreaks in which stool collection kits were deployed included 5 outbreaks (29%) in which specimens were not tested for the suspected pathogen, and 3 outbreaks (18%) in which kits were returned to the laboratory >10 days after onset of symptoms.

Table 1. Stool collection kit utilization in investigations of outbreaks of infections with and without confirmed etiologies.

Factor	Outbreaks of infections with confirmed etiology ($n = 37$)	Outbreaks of infections without confirmed etiology ($n = 17$)	P
Total no. of stool collection kits deployed	200	63	NA
Median no. of ill persons per outbreak	16	8	.1
Median no. of kits returned per outbreak	4	3	.41
Time from symptom onset to receipt of kit at laboratory, mean days	6.3	8.3	.13
No. (%) of kits returned by commercial carrier	95 (52)	20 (32)	.005
No. (%) of kits returned by mail	38 (21)	21 (33)	.049
No. (%) of kits returned by health department or laboratory courier	37 (20)	19 (30)	.12
No. (%) of kits returned by the patient	9 (5)	3 (5)	.95

NOTE. Mode of delivery was unknown for 19 kits. NA, not applicable.

Each stool collection kit took ~5 min to assemble and cost ~$7. The average cost of delivery of kits by commercial courier to patient homes or the pubic health laboratory was ~$18 per delivery. Average cost of delivery of kits by US mail was $2 per delivery. The average cost of delivery of kits by health department or laboratory courier was $12 per delivery.

Follow-up interviews were conducted with 228 (66%) of the 347 persons to whom stool kits were delivered. Kits had been received at the laboratory from 196 (86%) of the 228 persons interviewed. Ninety-six percent of persons interviewed stated that the instructions were clear and easy to use. Among the 32 persons interviewed who received a kit but did not subsequently submit a specimen, 20 (63%) stated that they could not produce a specimen or that their symptoms had resolved, and the rest cited various reasons, such as going out of town, forgetting, and "not wanting to deal with it." Local and state health departments reported that the kits were well received by health department staff who used them. Local investigators reported that the kits were convenient, simple, and easy to implement.

DISCUSSION

This pilot test of prepackaged, self-contained stool collection kits delivered to and picked up from patients markedly improved delivery of stool specimens to appropriate laboratories. The proportion of outbreaks of infection with a confirmed etiology in our study (69%) is markedly higher than the national average (37%) during the past decade. Although our findings should be interpreted with caution because we studied only a small number of outbreaks, the observation that noroviruses accounted for a majority of confirmed outbreaks of infection (76%) is also notable. Nationally, a low proportion of outbreaks of infection have been attributed to noroviruses, suggesting that the proportion of outbreaks caused by this agent is substantially underascertained. Importantly, the stool collection kits and procedures used in this study were well accepted by both patients and health department staff and were implemented at reasonable cost. Delivery of stool collection kits can be a practical means of increasing the number of foodborne disease outbreaks with a confirmed etiology.

Community surveys indicate that the majority of persons with diarrheal disease do not seek medical care, and the majority of those who do seek medical care do not submit a stool specimen for testing [9]. Not surprisingly, reports of outbreak investigations also suggest that the majority of persons associated with outbreaks do not submit a stool specimen for testing. Although recommendations exist [10], in many jurisdictions, collection of specimens during foodborne disease outbreak investigations is a haphazard and marginally successful endeavor. In Tennessee, for example, it is typical for local investigators to ask patients to come to the health department to pick up a stool collection container, which is dispensed with verbal instructions, and the patient is required to return the specimen to the health department. Rates of return of specimens are often well below 10%, and those that are returned have often been inappropriately packaged or handled (authors' unpublished data). The stool collection kits used in our study were assembled entirely from commercially available components, required no special expertise or education to deploy or use, and were easily mailed or delivered to patients. The primary advantage of the kits used in this study is that all materials, including instructions and prepaid shipping labels, are packaged conveniently and compactly for efficient storage, transportation, and use by both investigators and patients during outbreaks. Although we are not aware of studies identifying specific reasons for poor success in collecting stool specimens during outbreaks, the attributes of the kits used in this study appear to have overcome many of the likely barriers.

Delivery of kits to and from patients substantially improves the convenience of providing a specimen and appears to markedly increase the proportion of patients with specimens received at the appropriate laboratory. Several options for delivering kits to and from patients are available, including use of health department staff. In typical outbreak investigations, use of limited health department staff for specimen transportation draws them away from other important tasks and can be difficult to coordinate. Furthermore, when ill persons associated with an outbreak are located over a large geographic area or are out of state, use of health department staff for specimen delivery becomes less practical and more expensive. In most urban areas of the United States, commercial couriers are available for immediate door-to-door delivery of packages at any hour. We found that, if these services were used in defined areas and with health department oversight, commercial couriers were very convenient and well accepted at reasonable cost. When patients were widely dispersed and/or resided in rural areas, use of commercial couriers was infeasible. In those situations, we sent kits by Federal Express, and kits were returned to the appropriate laboratories by mail. Although mail transportation potentially led to several days of delay in receipt at the laboratory, as well as handling at uncontrolled temperatures, pathogens were successfully identified from mailed specimens, demonstrating that use of mail was preferable to an absence of specimens.

Because of the wide variation in methods of transportation and handling of stool collection kits, average cost per specimen collected could be estimated only roughly. Of importance, the cost of the kits themselves was judged to be marginally more that the materials routinely provided at a health department. The increased costs of our approach are the delivery costs, which we judged to be reasonable given the information obtained. In California, for example, the courier costs per outbreak ranged from $0 to $215, with an average cost per spec-

imen received of $43. Because collection of even a limited number of specimens will allow confirmation of the etiologic pathogen in many outbreaks, and given the demands on health departments to determine the etiology of infections in outbreaks, these costs are likely to be considered reasonable for markedly increasing the proportion of outbreaks of infection with a confirmed etiology.

In some areas, lack of accessible and reliable laboratory testing for viruses may contribute to the high proportion of outbreaks of foodborne disease without a confirmed etiology [11]. In states participating in this pilot project, molecular assays for noroviruses were available free of charge at public health laboratories. We found that noroviruses accounted for 52% of all outbreaks and 76% of outbreaks of infection with a confirmed etiology. These data suggest that, as molecular testing for noroviruses becomes more widely available, the proportion of outbreaks attributed to norovirus will increase, and the rates of detection of an etiologic agent in outbreaks of foodborne infection will improve.

Even with implementation of these stool collection kit procedures supported by well-equipped public health laboratories, an etiology was not confirmed in the infections in one-third of outbreaks. This finding highlights that efforts must continue to promptly collect sufficient numbers of specimens and to improve other aspects of outbreak investigations, including improving the accessibility of reliable laboratory testing for likely etiologic agents and collection of thorough environmental and epidemiological data that can be correlated with clinical and laboratory information. In our study, the majority of persons who received kits but did not submit a stool specimen reported that their diarrhea had resolved by the time collection was attempted, suggesting that facilitation of prompt collection remains a priority for improvement.

This study had substantial limitations. Slightly different stool collection kits and various methods of delivery were used in each participating state. Local procedures for investigation of outbreaks of foodborne diseases likely varied substantially and were not standardized during this study. The study was not controlled, and routine investigative measures (such as collection of specimens directly from patients seen in health department clinics and collection of environmental specimens) continued concurrently with the introduction of the kits. Few data exist on the sensitivity and specificity of particular transport media under different conditions and for different pathogens, and this study was not designed to assess such characteristics. Similarly, this study was not designed to determine the effect of various methods of transportation or delays in delivery on isolation rates of different pathogens.

Despite these limitations, this pilot study demonstrates that use of self-contained stool collection kits delivered to and from patients can be a practical and effective approach to improving investigations of foodborne disease outbreaks. Although there are many barriers to confirming the etiology of infection in an outbreak, this is the first study to examine a specific method for overcoming the primary obstacle of failure to collect adequate clinical specimens for laboratory testing. The use of stool collection kits to aid outbreak investigations should be possible for many jurisdictions at reasonable cost with few disadvantages compared with standard methods. Additional studies to further refine recommendations for wider implementation of stool collection procedures would be useful.

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Potential conflicts of interest. All authors: No conflict.

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